

Claims

What is claimed is:

- 5 1. An apparatus for measuring flow rates of a liquid in a capillary system comprising:
- a flow-divider;
- a main flow path carrying liquid to said flow-divider;
- an operating flow path carrying a first portion of said liquid from said flow-
- 10 divider according to a split ratio;
- a waste flow path carrying a second portion of said liquid from said flow-divider;
- a main flow sensor operatively disposed in said main flow path and configured to measure volumetric flow rates of said liquid in said main flow path to produce a main flow signal;
- 15 a restrictor disposed in said waste flow path defining said split ratio;
- a waste flow sensor operatively disposed in said waste flow path between said flow divider and said restrictor and configured to measure volumetric flow rates of said liquid in said waste flow path to produce a waste flow signal;
- a subtractor receiving said main flow signal from said main flow sensor and said
- 20 waste flow signal from said waste flow sensor and providing a difference signal representing a difference between said main flow signal and said waste flow signal; and
- a divider receiving said difference signal and said main flow signal and providing a quotient signal representing said split ratio of said flow-divider.
- 25 2. The apparatus according to claim 1 wherein said capillary system comprises a high pressure liquid chromatography (HPLC) system having operating stream flow rates in a range of approximately 50 nL/min to approximately 100 μ L/min.
- 30 3. The apparatus according to claim 1 wherein said main flow sensor and said waste flow sensor comprises a thermal-type flow sensor.

4. The apparatus according to claim 3 wherein said thermal-type flow sensor comprises:

means for introducing heat in a flow path;

5 means for measuring temperature of liquid in said flow path upstream and downstream of said means for introducing; and

means for computing volumetric flow rate of liquid in said flow path according to temperature changes measured upstream of said means for introducing compared to temperature changes measured downstream of said means for introducing in response to introduction of said heat.

10 5. The apparatus according to claim 1 wherein at least one of said main flow sensor and said waste flow sensor comprises a pressure-type flow sensor.

15 6. The apparatus according to claim 5 wherein said pressure-type flow sensors comprise:

restrictor means disposed in a flow path;

means for measuring fluid pressure upstream and downstream of said restrictor means; and

20 means for computing volumetric flow rate of liquid in said flow path according to a difference between pressure measured upstream of said restrictor means and pressure measured downstream of said restrictor means.

25 7. The apparatus according to claim 1 wherein said subtractor comprises an electronic subtraction circuit and wherein said divider comprises an electronic divider circuit.

8. The apparatus according to claim 1 wherein said quotient signal is used to control flow rate in an operating stream.

9. The system according to claim 1 further comprising a controller receiving said quotient signal from said divider and configured to adjust liquid flow rate in said operating flow path in response to said quotient signal.

5 10. The system according to claim 9 further comprising a waste path variable restrictor operatively disposed in said waste flow path and responsive to a signal from said controller to adjust said liquid flow rate in said operating flow path by varying permeability of said waste flow path.

10 11. The system according to claim 9 comprising a main path pump operatively disposed in said main flow path and responsive to a signal from said controller to adjust said liquid flow rate in said operating flow path by varying output pressure of said main path pump.

15 12. An apparatus for measuring nano-scale flow rates of a liquid in a high pressure liquid chromatography system comprising:
a flow-divider;
a main flow path carrying liquid to said flow-divider;
an operating flow path carrying a first portion of said liquid from said flow-
20 divider according to a split ratio;
a waste flow path carrying a second portion of said liquid from said flow-divider;
main sensor means operatively disposed in said main flow path and configured to measure volumetric flow rates of said liquid in said main flow path to produce a main flow signal;
25 a restrictor disposed in said waste flow path defining said split ratio;
waste sensor means operatively disposed in said waste flow path between said flow divider and said restrictor and configured to measure volumetric flow rates of said liquid in said waste flow path to produced a waste flow signal;
an electronic subtraction circuit receiving said main flow signal from said main
30 sensor means and said waste flow signal from said waste sensor means and providing a

difference signal representing the difference between said main flow signal and said waste flow signal;

an electronic divider circuit receiving said difference signal and said main flow signal and providing a quotient signal representing said split ratio of said flow-divider;

5 a controller receiving said quotient signal from said electronic divider circuit and adjusting the liquid flow rate in said operating flow path in response to said quotient signal; and

a waste path variable restrictor operatively disposed in said waste flow path and responsive to a signal from said controller to adjust said liquid flow rate in said operating
10 flow path by varying permeability of said waste flow path.

13. A method for measuring nano-scale flow rates of a liquid in a high pressure liquid chromatography (HPLC) system comprising:

measuring a main flow rate in a main flow path between an HPLC pump and a
15 flow-divider;

dividing said main flow path into an operating flow path and a waste flow path according to a split ratio of said flow-divider;

measuring a waste flow rate in said waste flow path;

subtracting said waste flow rate from said main flow rate to determine a flow rate
20 difference;

dividing said flow rate difference by said main flow rate to determine an empirical split ratio.

14. The method according to claim 13 wherein said empirical split ratio is
25 independent of varying liquid composition.

15. The method according to claim 13 further comprising:

adjusting the liquid flow rate in said operating flow path in response to said empirical split ratio.

16. The method according to claim 15 further comprising disposing a variable restrictor in said waste flow path and wherein said liquid flow rate in said operating flow path is adjusted by changing the permeability of said variable restrictor.

5 17. The method according to claim 15 wherein said step of adjusting involves adjusting liquid flow in said operating flow path by changing the output flow rate of said HPLC pump.

10 18. An apparatus for measuring flow rates of a liquid in a capillary system comprising:

a flow-divider;

a main flow path carrying liquid to said flow-divider;

an operating flow path carrying a first portion of said liquid from said flow-divider according to a split ratio of said flow-divider;

15 a waste flow path carrying a second portion of said liquid from said flow-divider;

a restrictor disposed in said waste flow path and defining said split ratio;

a main flow sensor operatively disposed in said main flow path and configured to measure volumetric flow rates of said liquid in said main flow path to produce a main flow signal;

20 an operating flow sensor operatively disposed in said operating flow path and configured to measure volumetric flow rates of said liquid in said operating flow path to produce an operating flow signal; and

a divider receiving said operating flow signal and said main flow signal and providing a quotient signal representing said split ratio of said flow-divider.